Original Article

# Dose–Effect Relationship of Motor Nerve Inexcitability on Outcome in Guillain–Barré Syndrome: A Prospective Cohort Study

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## Abstract

**Objective:** One or more inexcitable motor (IM) nerves are common during electrodiagnostic (EDx) study in Guillain–Barré syndrome (GBS). This study assessed the dose–effect relationship of IM nerves on outcome in patients with acute inflammatory demyelinating polyneuropathy (AIDP) and acute motor and/or sensory axonal neuropathy (AMAN and AMSAN). **Materials and Methods:** Eighty-eight GBS patients admitted during May 2018–June 2023 underwent detailed clinical evaluation and EDx study. Admission and follow-up disability were assessed on a 0–10 Clinical Grading Scale (CGS). Outcome was recovery at 6 months, defined as good (CGS <3) and poor (CGS ≥3). Binary multivariate logistic regression with backward elimination was used to calculate independent predictors of outcome. **Results:** Proportion of patients with complete recovery decreased significantly with increasing numbers of IM nerves ($P < 0.01$). Seventy-six patients were followed for 6 months. Among patients with IM nerves ($n = 28$), complete recovery was similar between AIDP and axonal GBS (70% vs. 50%, respectively; $P = 0.40$). However, in patients with recordable compound muscle action potentials (CMAPs) in all the motor nerves ($n = 26$), axonal GBS had significantly poor recovery compared to AIDP (75% vs. 9.1%; $P = 0.01$). Among patients receiving intravenous immunoglobulin (IVIg; $n = 42$), poor recovery was seen in 53.6% with IM nerves compared to 35.7% without ($P = 0.28$), while it was 37.5% versus 5.6% ($P = 0.04$), respectively, in those who did not receive IVIg ($n = 34$). However, only admission disability (odds ratio [OR] 0.88, 95% confidence interval [CI] 0.81–0.97; $P = 0.007$) was found to be an independent predictor of outcome. **Conclusion:** Although increasing numbers of IM nerves were associated with poor outcome on univariate analysis, they did not predict 6 months' outcome independently. Outcome did not differ between axonal GBS and AIDP among those with IM nerves. IVIg improved outcome in patients with IM nerves.

**Keywords:** AIDP, AMAN, axonal, Guillain–Barré syndrome, inexcitable motor nerves, mechanical ventilation, outcome

## Introduction

Guillain–Barré syndrome (GBS) is clinically characterized by acute flaccid quadriparesis/plegia.[1] Nerve conduction studies are vital for the diagnosis and prognostication. Electrophysiologically, two types of abnormalities can be seen: either demyelination or axonal, based upon which GBS has been classified as acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), and equivocal.[2] Axonal GBS (AMAN and AMSAN) and presence of inexcitable motor (IM) nerves on electrophysiological studies are uniformly associated with poor outcome.[3-6] IM nerves suggest severe and extensive damage to the nerves and could either be due to distal demyelination with conduction block, secondary Wallerian degeneration following demyelination, or primary and severe axonopathy.[7-12]

In patients with GBS, few motor nerves may be unrecordable (inexcitable), while others may show features of either axonal or demyelination. Motor nerve inexcitability of one or more peripheral motor nerves upon supramaximal stimulation during the first 2 weeks of GBS is seen in about 1.4%–19% of cases.[13-15] In a study, Triggs *et al*.[15] noted that GBS patients with one IM nerve had complete recovery at 1 year, while 50% of patients with three or more IM nerves had poor outcome. There is paucity of studies assessing the quantitative effect of IM nerves on outcome.[15] This prospective study aims to assess (1) the dose–effect relationship of the number of IM nerves and derive a cut-off above which poor outcome could be predicted and (2) whether presence of IM nerves influences the outcome in patients with AIDP and (AMAN and AMSAN).

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## Materials and Methods

Consecutive patients with GBS admitted at our center from May 2018 through June 2022 were included. This study was approved by the institute ethics committee (AIIMS/IEC/20/354), and the patient or his/her caregiver gave written informed consent.

### Inclusion criteria

All patients diagnosed with "classical" GBS, characterized by typical areflexic quadriparesis with or without sensory or cranial nerve involvement or dysautonomia,[16] were included in the study. GBS was diagnosed based on clinical, cerebrospinal fluid (CSF), and electrophysiological criteria.[17]

### Exclusion criteria

Patients with polio or non-polio enteroviral infections, acute transverse myelitis, porphyria, vasculitis, paralytic rabies, periodic paralysis, lymphoma with associated lymphomatous meningitis, leukemia, renal tubular acidosis, or those receiving chemotherapy, radiotherapy, or organ transplantation were excluded.

### Clinical evaluation

Detailed clinical history was obtained from the patients or their relatives. The demographic characteristics including duration of illness, time to peak disability, and preceding illness in the last 6 weeks were recorded. Respiratory failure needing mechanical ventilation (MV) was also noted. General and neurological examination included muscle tone, muscle power graded according to Medical Research Council (MRC) scale, reflexes, cranial nerve dysfunction, and sensory impairment. Patients were considered to have autonomic dysfunction if two or more bedside autonomic tests (sinus arrhythmia, resting tachycardia or bradycardia, sweating abnormality, constipation, postural hypotension, fluctuation in blood pressure) were positive. Admission disability was recorded as assessed on a 0–10 Clinical Grading Scale (CGS) [Supplementary Table 1].[18]

### Investigations

Investigations were done to exclude the mimickers as well as to confirm the diagnosis of GBS. They included blood leukocyte counts, hemoglobin, erythrocyte sedimentation rate, blood sugar, serum creatinine, protein and albumin, and serum electrolytes (sodium, potassium, calcium, magnesium, phosphorus). Human immunodeficiency virus (HIV) serology, radiograph of chest, and electrocardiogram were done in all the patients. CSF analysis was done for cell count, protein, and glucose. Motor nerve conduction study (NCS) including F-waves was done in bilateral peroneal, median, and ulnar nerves, while sensory NCS included bilateral median, ulnar, and sural nerves. All NCSs were done using standard techniques and compared with normative values using Neuropack X1 EP/EMG/NCV, MEB-2300 (Nihon Kohden, Tokyo, Japan). Distal and proximal compound muscle action potential (CMAP) amplitude (base to peak), distal motor latency (DML), proximal and distal CMAP duration, proximal/distal (p/d) CMAP amplitude and duration ratio, and motor nerve conduction velocity (MNCV) were assessed. In case of unrecordable CMAPs, we repeated NCS at higher sweep speed (10 msec/div) and increased stimulus duration. When no CMAP was recordable even at higher sweep speed and increasing stimulus duration, and from a proximal muscle, only then they were labeled as IM nerves. The first NCS was done within 24 h of admission. A definite partial conduction block was defined as p/d-CMAP ratio ≤0.5, with minimal temporal dispersion (TD; duration of the negative peak d-CMAP increase ≤30%). A probable partial conduction block was defined as an amplitude decrement of 40%–49% with <30% TD. These criteria were applied when d-CMAP was ≥20% lower limit of normal (LLN).[19] At least 10 F-wave responses were examined in each patient. An absent or blocked F response was defined as F-wave persistency <20% and was discounted if the d-CMAP amplitude was markedly reduced (<20% LLN) or absent. Sensory NCSs were performed antidromically and averaging of at least eight responses was performed to improve the signal-to-noise ratio. The amplitude of the sensory nerve action potential (SNAP) was measured from baseline to the negative peak. NCS was done by the same technician with required expertise in the same laboratory and was supervised by a neurologist (MK, AT). For motor conduction, stimulus duration of 0.1 ms, a sensitivity setting (gain) of 1–2 mV/division (100 μV/division for very low amplitudes), a sweep speed of 2 ms/division, and filtering from 5 Hz to 5 kHz were applied for all measurements, while for sensory conduction, gain of 10 μV/division, a sweep speed of 1 ms/division, and filtering from 20 Hz to 3 kHz were used. Limb temperature was kept at around 32°C–34°C. On the basis of clinical findings, the patients were categorized as pure motor and sensory motor GBS. Based on neurophysiological studies, patients were categorized as below.[2,20]

**AIDP:** ≥2 features of demyelination (prolonged DML, slowing nerve conduction velocity (NCV), conduction block (CB), or prolonged F-wave latency) in ≥2 nerves or ≥2 demyelinating features in one nerve, if all other motor nerves are inexcitable and distal CMAP is ≥10% LLN.[2]

**AMAN:** Motor NCS revealing reduced distal CMAP of less than 80% of LLN or unrecordable in more than two nerves with normal sensory conduction, without any demyelinating features (except one demyelinating feature allowed in one nerve if the distal CMAP is <10% of LLN).[2]

**AMSAN:** Motor NCS findings similar to AMAN plus SNAP amplitude (<50%) of LLN in ≥2 two nerves without the feature of demyelination.[20]

**Equivocal:** Abnormal NCS not fulfilling the above-mentioned criteria.

### Management

Intravenous immunoglobulin (IVIg) was prescribed to all the patients with moderate to severe disability who reported within 15 days at a dose of 400 mg/kg daily for 5 days. None received plasmapheresis (plasma exchange [PLEX]). Ours, being a

tertiary care teaching government hospital, basic treatment modalities are provided free of cost, including mechanical ventilator and intensive care unit (ICU)-related supplies, diet, physiotherapy, and nursing care. However, costly treatment like IVIg is not included under the basic treatment modalities, and hence patients must pay for the same. IVIg, however, is still costly for most of the middle-class families in India. Those below poverty line received IVIg under various government schemes. Patients with respiratory failure and those with autonomic dysfunction were admitted to ICU. They were intubated and mechanically ventilated if arterial blood gas (ABG) analysis revealed hypoxia ($PaO_2 < 60$ cm of $H_2O$), hypercarbia ($PaCO_2 > 52$ cm of $H_2O$), or acidosis (pH < 7.3).[21] Patients with bulbar weakness were fed by a nasogastric tube.

### Outcomes

Recovery at 6 months (±7 days) was defined as complete (CGS < 3) or poor (CGS ≥ 3). In-hospital death and its immediate cause were also noted.[21]

### Statistical analysis

Categorical data were presented as proportions, while continuous data were expressed as means and standard deviations if normally distributed and as medians and interquartile ranges (IQRs) if non-normally distributed. Differences in proportions were analyzed using Chi-square or Fisher exact tests, and Mann–Whitney U test or independent *t*-test was used for continuous variables. Cochran–Armitage trend test was used to assess changes over time. Differences in the median among multiple independent groups were compared using Kruskal–Wallis test. Receiver operating characteristic (ROC) curve was drawn to define the cut-off values for IM nerves for 6 months' outcome. To analyze overall survival, we plotted Kaplan–Meier curves and did the log-rank test to compare the outcomes of patients within IM nerves. The predictors of outcome at 6 months were evaluated using univariate analysis. Variables with $P < 0.1$ on univariate analysis were included in binary multivariate logistic regression with backward elimination to calculate the independent predictors of outcome. Statistical Package for the Social Sciences (SPSS) Statistics v23.0 and GraphPad Prism 5 were used for statistical analyses. A two-sided $P$ value < 0.05 was considered to be statistically significant.

**Data availability statement:** The data will be available from the corresponding author on reasonable request.

## Results

Eighty-eight patients with GBS were included in the study. All the patients had flaccid quadriparesis at presentation. The median age of the patients was 33 (range 6–74) years, and 59 (67%) patients were males. The duration of illness was 6 (range 1–25) days, and the median time from disease onset to start of treatment (IVIg) was 8 (range 2–15) days. Forty-two (47.7%) had sensorimotor and 46 (52.3%) had pure motor GBS. Fifty (56.8%) patients had AIDP, 12 (13.6%) had AMAN, three (3.4%) had AMSAN, 10 (11.4%) had equivocal, and 13 (14.8%) had unrecordable CMAPs in all nerves. There were 46 (52.3%) patients with one or more IM nerves, of which 11 (12.5%) patients had one, 15 (17%) had two, seven (8%) had four, and 13 (14.8%) had six IM nerves. The remaining 42 (47.7%) patients had recordable CMAPs in all the motor nerves examined.

### Comparison of baseline characteristics of patients with one or more IM nerves

Patients with six IM nerves had significantly lower MRC sum score (median 0, range 0–20) compared to those with less than six IM nerves ($P < 0.01$ for trend). MV was required in 19% patients with all recordable CMAPs, 45.5% patients with one IM nerve, 33.3% patients with two IM nerves, 42.9% patients with four IM nerves, and 92.3% patients with all six IM nerves ($P < 0.01$ for trend). Admission disability worsened significantly with increasing number of IM nerves ($P < 0.01$). There was no correlation between the number of IM nerves and the duration of illness (presentation). The median time from onset of symptoms to the first electrodiagnostic (EDx) was 7 (2–26) days. Twenty-two (25%) patients underwent NCS study within 4 days, 34 (38.6%) within 4–7 days, 22 (25%) within 7–14 days, and 10 (11.4%) after 14 days of disease onset, and the mean number of IM nerves was 1.41 ± 0.50, 1.53 ± 0.51, 1.45 ± 0.51, and 1.50 ± 0.53, respectively ($P = 0.88$). Comparison of baseline characteristics is presented in Table 1.

### Correlation of increasing number of IM nerves with 6 months' outcome: A dose–effect relationship

Twelve patients were lost to follow-up. Therefore, the outcome analysis is based on 76 patients. Four patients died in-hospital and were included as poor outcome. Complete recovery was seen in 26/32 (81.2%) patients with no IM nerves, 6/10 (60%) with one IM nerve, 11/14 (78.6%) with two IM nerves, 3/7 (42.9%) with four IM nerves, and 3/13 (23.1%) patients with six IM nerves ($P < 0.01$ for trend). Outcome was also compared with increasing numbers of IM nerves. Kaplan–Meier plots have been shown in Figure 1. ROC curve was drawn to define the best performing cut-off for the number of IM nerves for predicting 6 months' outcome. The area under the curve (AUROC) was 0.73. At a cut-off of 4, the sensitivity and specificity were 52% and 87.8%, respectively, while they were 37% and 93.9%, respectively, at a cut-off of 6 [Figure 2].

### Effect of treatment (IVIg) on 6 month's outcomes in patients with/without IM nerves

Out of 42 patients receiving IVIg, 22 (52.4%) had complete recovery compared to 27 out of 34 (79.4%) patients who did not receive IVIg ($P = 0.01$) showing complete recovery. This could be due to significantly higher admission disability among patients receiving IVIg.

Since some of our patients did not receive IVIg, the effect of IM nerves on outcome was compared for those who received IVIg with those who did not receive IVIg. Among 42 GBS patients (of 76 followed for 6 months) who received IVIg, 15/28 (53.6%) with ≥1 IM nerve had poor outcome compared to 5/14 (37.5%) without any IM nerve ($P = 0.28$). However,

in 34 patients who did not receive IVIg, 6/16 (37.5%) patients with ≥1 IM nerve had poor outcome compared to 1/18 (5.6%) patients without any IM nerve ($P = 0.04$).

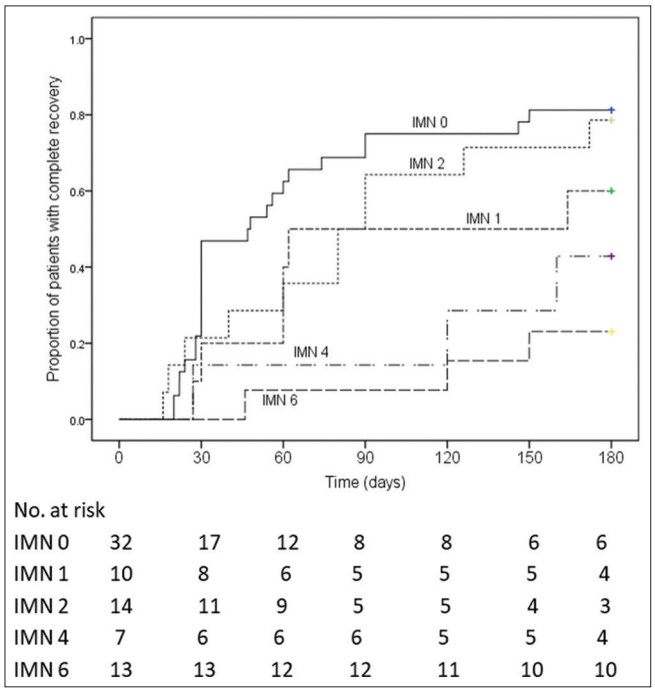


**Figure 1:** Kaplan–Meir plot showing proportion of patients with complete recovery at 6 months (patients who were lost to follow-up were excluded) ($P = 0.002$, using log-rank test)

## Effect of presence of one or more IM nerves on outcome among patients with axonal versus demyelinating GBS subtypes

Of 76 patients followed up for 6 months, 42 (55.3%) had AIDP and 12 (15.8%) had axonal neuropathy (AMAN and AMSAN). Of 54 patients (42 AIDP and 12 axonal), 26 (48.1%) had all

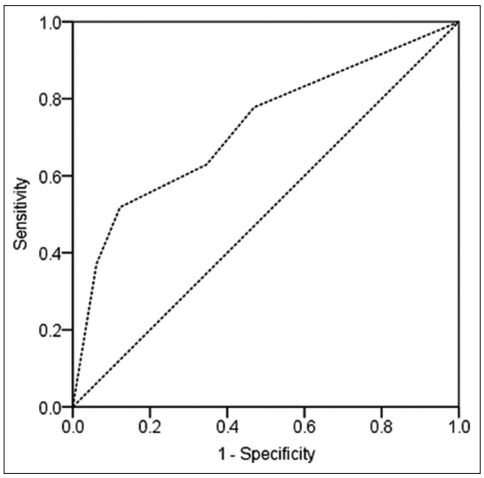


**Figure 2**: AUC for "number of inexcitable nerves" as a predictor of poor outcome at 6 months. AUC for poor 6 months' outcome was 0.73 (95% CI 0.60–0.85, $P < 0.01$). At a cut-off of four inexcitable motor nerves, the sensitivity and specificity were 52% and 87.8%, respectively, while they were 37% and 93.9%, respectively, at a cut-off of six inexcitable motor nerves . AUC = area under the receiver operating characteristic curve, CI = confidence interval

**Table 1: Comparison of baseline characteristics of patients with one and patients with more IM nerves**

| Characteristics | IM nerve 0 (*n*=42) | IM nerve 1 (*n*=11) | IM nerve 2 (*n*=15) | IM nerve 4 (*n*=7) | IM nerve 6 (*n*=13) | *P* |
|---|---|---|---|---|---|---|
| Age, median (range) | 30 (6–65) | 46 (18–63) | 33 (13–71) | 40 (9–62) | 40 (6–74) | 0.20 |
| Sex (male), *n* (%) | 29 (69.0) | 6 (54.5) | 10 (66.7) | 4 (57.1) | 10 (76.9) | 0.78 |
| DOI, median (range) | 6 (1–25) | 6 (2–17) | 7 (2–20) | 7 (5–15) | 4 (1–14) | 0.44 |
| Sensorimotor, *n* (%) | 19 (45.2) | 7 (63.6) | 9 (60.0) | 1 (14.3) | 6 (46.2) | 0.26 |
| NCS subtypes, *n* (%) | | | | | | |
| AIDP | 29 (69) | 8 (72.7) | 11 (73.3) | 2 (28.6) | 0 (0.0) | <0.01 |
| AMAN | 5 (11.9) | 1 (9.1) | 1 (6.7) | 5 (71.4) | 0 (0.0) | |
| AMSAN | 1 (2.4) | 1 (9.1) | 1 (6.7) | 0 (0.0) | 0 (0.0) | |
| Equivocal | 7 (16.7) | 1 (9.1) | 2 (13.3) | 0 (0.0) | 0 (0.0) | |
| IMN (all motor nerves) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 13 (100) | |
| Bulbar, *n* (%) | 17 (40.5) | 6 (54.5) | 7 (46.7) | 3 (42.9) | 11 (84.6) | 0.02* |
| Facial, *n* (%) | 18 (42.9) | 7 (63.6) | 7 (46.7) | 4 (57.1) | 6 (46.2) | 0.78* |
| Dysautonomia, *n* (%) | 14 (33.3) | 6 (54.5) | 6 (40.0) | 3 (42.9) | 11 (84.6) | <0.01* |
| MV, *n* (%) | 8 (19.0) | 5 (45.5) | 5 (33.3) | 3 (42.9) | 12 (92.3) | <0.01* |
| Admission CGS, median (range) | 7 (3–9) | 7 (6–8) | 7 (3–8) | 8 (8–8) | 8 (8–9) | <0.01 |
| Admission MRC sum score, mean±SD | 28±15.0 | 25±13.3 | 29±15.2 | 14±11.5 | 5±7.4 | <0.01 |
| IVIg, *n* (%) | 22 (52.4) | 7 (63.6) | 8 (53.3) | 4 (57.1) | 11 (84.6) | 0.33 |
| CSF cells, median (range) | 5 (0–5) | 5 (2–15) | 5 (4–8) | 5 (3–15) | 0 (0–5) | 0.24 |
| CSF protein, median (range) | 101 (51–174) | 150 (51–245) | 72 (48–153) | 70 (45–258) | 70 (44–139) | 0.81 |
| Liver dysfunction, *n* (%) | 11 (26.2) | 5 (45.5) | 8 (53.3) | 3 (42.9) | 2 (15.4) | 0.72* |

*Test for trend using Cochrane–Armitage test. AIDP=Acute inflammatory demyelinating polyradiculoneuropathy, AMAN=acute motor axonal neuropathy, AMSAN=acute motor axonal neuropathy, CGS=Clinical Grading Scale, CSF=cerebrospinal fluid, DOI=duration of illness, IM=inexcitable motor, IMN=inexcitable motor nerve (all), IVIg=intravenous immunoglobulin, MRC=Medical Research Council, MV=mechanical ventilation, NCS=nerve conduction study

**Table 2: Univariate and multivariate regression analyses for predictors of good (CGS 0–2) and poor (CGS 3–10) outcome at 6 months (*n*=76)**

| Characteristics | Good outcome (*n*=49) | Poor outcome (*n*=27) | *P* (univariate analysis) | Adjusted OR* (95% CI) | Adjusted *P** |
|---|---|---|---|---|---|
| Age, median (range) | 30 (6–65) | 40 (9–74) | 0.16 | - | - |
| Sex (male), *n* (%) | 35 (71.4) | 16 (59.3) | 0.28 | - | - |
| IVIg, *n* (%) | 22 (44.9) | 20 (74.1) | 0.01 | 0.91 (0.20–4.23) | 0.91 |
| Sensorimotor, *n* (%) | 27 (55.1) | 10 (37.0) | 0.13 | - | - |
| IM nerves, mean±SD | 3.2±2.5 | 1.2±1.7 | <0.01 | 1.01 (0.71–1.43) | 0.97 |
| Number of IM nerves, *n* (%) | | | | | |
| 0 | 26 (53.1) | 6 (22.2) | <0.01 | - | - |
| 1 | 6 (12.2) | 4 (14.8) | 0.74 | | |
| 2 | 11 (22.4) | 3 (11.1) | 0.36 | | |
| 4 | 3 (6.1) | 4 (14.8) | 0.24 | | |
| 6 | 3 (6.1) | 10 (37.0) | <0.01 | | |
| Electrophysiological subtype, *n* (%) | | | | | |
| AIDP | 34 (69.4) | 8 (29.6) | <0.01 | - | - |
| AMAN | 4 (8.2) | 6 (22.2) | | | |
| AMSAN | 1 (2.0) | 1 (3.7) | | | |
| Equivocal | 7 (14.3) | 2 (7.4) | | | |
| All IMN | 3 (6.1) | 10 (37.0) | | | |
| Dysautonomia, n (%) | 18 (36.7) | 17 (63.0) | 0.03 | - | - |
| Bulbar, *n* (%) | 19 (38.8) | 19 (70.4) | <0.01 | - | - |
| Facial, *n* (%) | 21 (42.9) | 15 (55.6) | 0.29 | - | - |
| MV, *n* (%) | 12 (24.5) | 20 (74.1) | <0.01 | 2.1 (0.48–9.53) | 0.32 |
| Admission CGS, median (range) | 7 (3–9) | 8 (7–9) | <0.01 | 0.88 (0.81–0.97 | 0.007 |
| Admission MRC sum score, mean±SD | 31±12.8 | 9±12.6 | <0.01 | 1.26 (0.40–3.9) | 0.69 |
| DOI, median (range) | 6 (1–25) | 5 (1–14) | 0.09 | 1.09 (0.91–1.32) | 0.35 |

*Binary multivariate logistic regression analysis. AIDP=acute inflammatory demyelinating polyradiculoneuropathy, AMAN=acute motor axonal neuropathy, AMSAN=acute motor axonal neuropathy, CGS=Clinical Grading Scale, CI=confidence interval, DOI=duration of illness, IMN=inexcitable motor nerve (all), IVIg=intravenous immunoglobulin, MRC=Medical Research Council, MV=mechanical ventilation, OR=odds ratio, SD=standard deviation

nerves with recordable CMAPs and 28 (51.9%) had one or more IM nerves. Among patients with all recordable CMAPS (*n*=26), three out of total four (75%) patients with axonal GBS had poor recovery compared to two out of 22 (9.1%) with AIDP (*P*=0.01). However, among 28 patients with one or more IM nerves, four out of eight patients (50%) with axonal GBS had poor recovery compared to six out of 20 (30%) with AIDP (*P*=0.40).

### Independent predictors of 6 months' outcome

Admission disability (CGS), admission MRC sum score, number of IM nerves, IVIg, duration of illness, and need for MV were included in the binary multivariate logistic regression analysis with backward elimination to assess independent predictors of 6 month's outcome. Only admission disability (odds ratio [OR] 0.88, 95% confidence interval [CI] 0.81–0.97; *P*=0.007) was found to be an independent predictor of outcome [Table 2].

## Discussion

In the present study, a linear relationship was observed, with patients having higher numbers of IM nerves significantly more likely to have worse outcome at 6 months. We found that patients with a cut-off of ≥4 IM nerves had significantly worse outcome compared to those with <4 IM nerves, with sensitivity of 52% and specificity of 87.8%. Cut-off of ≥6 IM nerves had lower sensitivity (37%) with similar specificity (93.9%) as for a cut-off of ≥4. Hence, four or more IM nerves was considered as the best trade-off with a positive predictive value (PPV) of 70% and a negative predictive value (NPV) of 76.8%. The cut-off definition is similar to those reported in the previous studies.[2,15] In a cohort of eight GBS patients, Triggs *et al*.,[15] noted that all the patients with one IM nerve had complete recovery at 1 year, while 50% of patients with ≥3 IM nerves had poor outcome. Similarly, in another study where four motor nerves were tested, it was shown that 50% and 63% of patients with all four IM nerves at the first and second NCS (median 36 days apart), respectively, had poor outcome.[2] In our study, 70% of patients with ≥4 IM nerves had poor outcome, which is comparable to that reported in the above studies.

Previous studies have shown that axonal GBS (AMAN and AMSAN) is uniformly associated with poor recovery compared to AIDP.[3-6] In the present study, the traditional view that the axonal form of GBS has poor recovery compared to AIDP was seen only in patients with all recordable CMAPs. On the contrary, outcome did not differ between axonal and AIDP among those with IM nerves. One plausible explanation of this finding may be that the presence of IM nerves might have resulted in poor recovery in patients with AIDP, which

otherwise has better prognosis compared to the axonal variant. This is evidenced by the fact that only 70% of AIDP patients with IM nerves showed complete recovery at 6 months, compared to 90% without any IM nerves. Motor nerve inexcitability in GBS could be due to either distal demyelination with conduction block or secondary Wallerian degeneration following extensive primary proximal demyelination or severe primary axonopathy.[7-12] In any case, presence of IM nerves suggests extensive nerve damage.[2,6,15] However, although increasing numbers of IM nerves were associated with poor outcome on univariate analysis, they did not predict 6 months' outcome independently. Only disability (CGS) at admission was found to be an independent predictor of outcome at 6 months. Furthermore, IVIg could mitigate the deleterious effect of IM nerves on the outcome. In our study, we found that among patients who did not receive IVIg, presence of IM nerves was associated with significantly worse outcome compared to that in those who had all recordable motor nerves. On the contrary, outcome was similar in patients receiving IVIg with and without IM nerves, who received IVIg. It must, however, be noted that patients receiving IVIG had more severe disease at baseline compared to those who did not receive IVIg.

We performed single NCS, and it may be possible that many patients with AMAN with reversible conduction failure (RCF) may have been misdiagnosed as AIDP. Patients with AMAN with RCF show rapid recovery,[22] and hence could have influenced the overall study results. However, apart from the possible detection of RCF, the value of repeated NCS is currently debated.[23-27] In addition, instead of Hadden's criteria, a stricter criterion, such as the one proposed by Rajabally *et al*.,[28] could have better characterized electrophysiological subtypes on single NCS. However, while Rajabally's criteria are highly sensitive for diagnosing axonal GBS, they are difficult to diagnose AIDP.[20,23]

The cut-off definition of four or more IM nerves in our study may help redefine the criteria of inexcitable motor nerve (IMN), an electrophysiological subtype in GBS, defined as those patients "with either absent CMAP in all motor nerves or present in only one nerve with CMAP <10% of LLN."[2] The current definition lacks uniformity as different studies have examined different numbers of motor nerves (range 3–6).[2,6,14,15,21] Thus, the number of nerves required to be labeled as IMN is lacking. For example, a patient in whom only three motor nerves are examined with all nerves unrecordable will be classified as IMN according to the current definition, even though the same patient would have been classified into another electrophysiological subtype, had more than three nerves been examined, with few of them showing recordable CMAPs. Thus, it may be suggested that at least four motor nerves be examined in any GBS patient for better prognostication. This finding, however, needs further validation in a large cohort of patients.

**Limitations:** This study is limited by lack of serial NCSs, and it may be possible that many patients with AMAN with RCF may have been missed. This could have influenced the outcome as AMAN with RCF shows rapid recovery. Another limitation of the study is its small sample size. In addition, we had no patients with NCS showing either three or five IM nerves. Also, although IVIg was prescribed to all, some of them could not afford the treatment as patients had to pay out of their pocket. This had a bearing on the outcome of the patients.

## Conclusion

Although increasing numbers of IM nerves were associated with poor outcome on univariate analysis, they did not predict 6 months' outcome independently. Outcome did not differ between axonal GBS and AIDP among those with IM nerves. IVIg improved outcome in patients with IM nerves.

### Ethical approval

This study was approved the by Institutional Ethics Committee. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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**Supplementary Table 1: CGS for assessment of severity of Guillain–Barré syndrome**

| Grade | Characteristics |
|---|---|
| Grade 0 | Normal |
| Grade 1 | No disabilities, minor sensory signs, or areflexia |
| Grade 2 | Mild disability, ambulatory for >200 m, mild weakness in one or more limbs, mild sensory signs or symptoms |
| Grade 3 | Moderate disability, ambulatory for >50 m without stick, MRC grade 4 weakness, and sensory impairment |
| Grade 4 | Severe disabilities; able to walk more than 10 m, marked motor and sensory signs |
| Grade 5 | Requires support to walk 5 m, marked motor and sensory signs |
| Grade 6 | Cannot walk 5 m, able to stand unsupported and transfer to wheelchair, able to feed independently |
| Grade 7 | Bed ridden, severe quadriparesis, maximum MRC grade 3 |
| Grade 8 | Respiratory impairment and/or quadriparesis, maximum MRC grade 2 |
| Grade 9 | Needs respirator and quadriplegia (MRC grade 0, 1) |
| Grade 10 | Dead |

CGS=Clinical Grading Scale, MRC=Medical Research Council